IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	**09/643,686**
Applicants	:	Gerald QUAPIL et al.
Title	:	DEVICE FOR ANALYZING IMMUNOASSAYS
Filed	:	August 24, 2000
Art Unit	:	1641
Examiner	:	Kartic Padmanabhan
Docket No.	:	31833-150836
Customer No.	:	26694

Commissioner for Patents
P.O. Box 1450
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RULE 116 AMENDMENT

In response to the Final Office Action dated June 15, 2004, Applicants submit the following Amendment and Reply. A Notice of Appeal is being submitted herewith along with a request for a Three (3) Month Extension of Time. The Application is amended as follows:

Amendments to the Claims are reflected in the listing of the claims which begins on page 2.

Remarks begin on page 8.

The requisite fees should be charged to Deposit Account No. 22-0261.

Amendment to the Claims:

The listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims:

Claim 1 (canceled).

Claim 2 (Previously presented): The device according to claim 27, wherein the base of the vessel has a second side wall arranged opposite from the first side wall, wherein both the first and second side walls are flat and extend at an angle of less than 90° to the boundary surface, the transmitted light rays are coupled into the base via the first side wall and, following a total reflection at the boundary surface, are coupled out via the second side wall.

Claim 3 (Original): The device according to claim 2, wherein the first and second side walls of the base extend symmetrically to a symmetry plane of the base.

Claim 4 (Original): The device according to claim 2, wherein the vessel has an essentially hollow-cylindrical shape, the base is circularly cylindrical, and the first and second sidewalls comprise sloping sides for the circularly cylindrical base.

Claim 5 (Previously presented): The device according to claim 27, wherein each of the vessels has an open top presenting an upper edge, and the device further includes a disk-shaped attachment adjoining the upper edge for facilitating insertion of the vessel into a holder.

Claim 6 (Original): The device according to claim 5, wherein the attachment has a rectangular cross section presenting longitudinal sides that can be attached to the holder.

Claim 7 (Previously presented): The device according to claim 5, wherein the attachment has one side edge for receiving a marking characterizing the content of the vessel.

Claim 8 (Previously presented): The device according to claim 5, wherein the vessels and attachment comprise one piece.

Claim 9 (Previously presented): The device according to claim 27, wherein each of the vessels comprises an injection-molded plastic part.

Claim 10 (Previously presented): The device according to claim 9, wherein the vessels are comprised of polystyrene.

Claim 11 (Previously presented): The device according to claim 27, wherein the transmitters are arranged so that the transmitted light rays outside of the vessel extend parallel to the boundary surface of the vessel.

Claim 12 (Previously presented): The device according to claim 27, wherein the base has an underside and the receiver is arranged so that the at least one of the fluorescent rays and phosphorescent rays are coupled out via the underside of the base and conducted to the receiver.

Claim 13 (Previously presented): The device according to claim 27, further comprising an optical swamp arranged so that the light rays transmitted into the base via the first side wall are conducted to the optical swamp after the light rays exit from the vessel.

Claim 14 (Previously presented): The device according to claim 27, wherein each of the transmitters comprises a laser and a polarization filter connected downstream of the laser.

Claim 15 (Previously presented): The device according to claim 13, further comprising an arrangement of mirrors and upstream connected polarization filters for transmitting the light rays repeatedly through the bases of the vessels and onto the boundary surface.

Claim 16 (Previously presented): The device according to claim 27, wherein the transmitter is operable in a pulsed mode having a pulse-break ratio of transmitting light pulses selected such that optically excited luminophores emit fluorescent rays during emission of a transmitting light pulse and emit phosphorescent rays during transmitting breaks.

Claim 17 (Previously presented): The device according to claim 16, wherein the different luminophores include first and second luminophores, the first luminophores having a high fluorescence and low phosphorescence and the second luminophores having high phosphorescence and a low fluorescence.

Claim 18 (Previously presented): The device according to claim 16, wherein the receiver detects the first reaction agents with a time delay such that the fluorescent rays from the first luminophores are recorded during the emission of the transmitting light pulses and the phosphorescent rays from the second luminophores are recorded during the transmitting breaks.

Claim 19 (Previously presented): The device according to claim 27, wherein the receiver is one of a photo-multiplier, a PIN detector, and an avalanche diode, and includes a polarization filter, a receiving optic, and an interference filter installed in front of the receiver.

Claim 20 (Canceled).

Claim 21 (Canceled).

Claim 22 (Previously presented): The device according to claim 27, wherein the vessels are arranged in a linear arrangement of vessels.

Claim 23 (Previously presented): The device according to claim 27, further including a polygonal mirror and wherein the vessels are arranged concentrically to the polygonal mirror so that the fluorescent rays exiting at the vessels are conducted via the polygonal mirror to the receiver.

Claim 24 (Withdrawn): A method for analyzing immunoassays with a liquid medium comprising:

utilizing the device of claim 27; and

operating the transmitters for transmitting light pulses in a pulsed mode, the pulsed mode having a pulse-break ratio, the pulse-break ratio being selected such that optically excited luminophores emit fluorescent rays during emission of a transmitting light pulse and emit phosphorescent rays during transmitting breaks.

Claim 25 (Withdrawn): The method according to claim 24, further comprising:

labeling two different reaction agents with different luminophores, wherein the first luminophores have a high fluorescence and low phosphorescence and the second luminophores have high phosphorescence and a low fluorescence.

Claim 26 (Withdrawn): The method according to claim 24, further comprising:

detecting the first reaction agents with a time delay;

recording fluorescent rays from first luminophores during the emission of the transmitting light pulses; and

recording phosphorescent rays from second luminophores during the transmitting breaks.

Claim 27 (Currently presented): A device for analyzing sandwich immunoassays with a liquid assay

medium, comprising:

a vessel for holding the assay medium, the vessel having a base comprised of a solid body, the solid body having a first side wall and a top surface constituting a bottom surface of the vessel and forming a boundary surface of the solid body, wherein first reaction agents are dissolved in the assay medium in the vessel and are labeled with a luminophore or different luminophores and second reaction agents are bonded to the boundary surface within a boundary layer of the assay medium;

a transmitter for emitting light rays that are coupled into the base of the vessel via the first side wall and conducted at a total reflection angle to the boundary surface so that luminophore-labeled first reaction agents that are bonded to the second reaction agents are optically excited by at least some of the light rays and emit at least one of fluorescent and phosphorescent rays; and

a receiver positioned for quantitatively detecting the at least one of the fluorescent rays and phosphorescent rays,

wherein the transmitter comprises a plurality of transmitters activated individually, one after another, and the vessel comprises a multiple arrangement of vessels onto which light rays emitted by the transmitters are respectively focused, and the receiver is a common receiver for recording the fluorescent rays exiting from the individual vessels.

Claim 28 (New): A device for analyzing immunoassays with a liquid assay medium, comprising:

a vessel having a well with a lower portion for holding the assay medium and having a base which has a top layer that defines the lower portion of the well and a first side wall, which is capable of receiving light rays and reflecting them to the top layer where a second reaction component is bound;

a transmitter for emitting light rays to the base of the vessel via the first side wall and conducted at a total reflection angle to a boundary surface formed between the bound second reaction component and the assay medium so that luminophore-labeled first reaction agents that are bonded to the second reaction agents are optically excited by at least some of the light rays and emit at least one

of fluorescent and phosphorescent rays;

a receiver positioned functionally below the base for quantitatively detecting the at least one of the emitted fluorescent rays and phosphorescent rays; and

optionally an optical swamp positioned functionally below the base to receive the reflected light rays, wherein the assay medium contains first reaction agents which are labeled with a luminophore or different luminophores and sample suspected of containing an analyte of interest.

Remarks

Entry of the amendment is respectfully requested since it would reduce the issues on appeal and is believed to be fully supported by the application as fiied.

Upon entry of the amendment Claims 2-19, 22-23, 27 and 28 are pending in the application, with claims 27 and 28 being independent claims. Claims 24-26 have been withdrawn from consideration. Claim 27 has been amended to clearly indicated in the preamble the nature of the immunoassay set forth in the body of the claim, e.g. "sandwich". Claim 28 has been added to more clearly set forth inventive aspects of the invention.

Based on the present Amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

This Amendment is being submitted concurrently with a Notice of Appeal.

Rejections under 35 U.S.C. § 103

Claims 2-19, 22-23 and 27 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Lekkala et al. (WO 95/22754) in view of Babson et al. (U.S. Patent No. 5,885,530). Applicants respectfully traverse.

Lekkala et al. describes a device and method which relies on a different assay formula than that claimed and disclosed. Lekkala et al. does not employ labels and does not employ conditions which result in the formation of antibody-antigen-antibody complex. See page 6 starting at line 20. Lekkala et al. measures a difference in reflected light due to a resonance phenomenon. The resonance phenomenon relied upon by Lekkala et al. amplifies the so-called evanescent electric field, which is generated in the total reflection. A evanescent field, created by a light source, "sees" the reaction taking place on the reaction surface (material layer), e.g. the formation of a complex between the antibody bound on the material layer and the antigen analyt in the sample, because the reaction

correspondence to a definite change of the refraction index, due to the formed complex, on the surface of the material layer. The degree of binding can be measured from the reflected light because resonance (disappearance of light) is shifted to another value of incident angle. See page 3 starting at line 26. The measurement based on this SPR phenomenon is conducted from the direction of the bottom of the structure through a suitable prism structure. If one contrasts the figures of the instant application with those of Lekkala et al., e.g. figures 2a-2c and 4a-b, one can readily see the differences in the measurement mechanism. Lekkala et al. measures the degree of binding due to a loss in the reflected light. The instant invention measures the florescence or phosphorescence due to the bound label at an angle distinct from that of the reflect light beam. See, for example, instant Figure 1. This different assay protocol necessitates different positioning of device elements, e.g. receiver (10) relative to those of Lekkala et al.

Babson et al. patent has been reviewed. It is not seen how it remedies the deficiencies of Lekkala et al., noted above. While Babson et al. does teach an automated immunoassay analyzer, this analyzer is not based on either the Lekkala et al. SBR based assay or the sandwich assay device claimed. There is no mention of the SPR or an equivalent phenomenon nor is the Babson et al. device set up to measure light differences like those disclosed by Lekkala et al. Babson et al. employ a traditional heterogeneous immunoassay format. The Babson et al. substrate for the immobilized phase are a collection of beads and not the bottom surface of an assay well. The Babson et al. measurement mechanism and device is distinct from that used either for Lekkala et al. SPR based device or that claimed.

The propriety of the reference combination is questioned. It is not seen how or why one would combine the references. There is no apparent problem in either reference for which the other provides a solution. There is not even a similarity in assay format. Lekkala et al. teaches as an advantage the absence of labels. Babson et al. employs labels. Further, the use of labels in Lekkala et al. assay format would necessitate changes in the measuring device. There is no guidance as to how the requisite changes would be made. There is no motivation referred to in the Office Action

which would suggest why the changes would be made, even if they were taught.

It is respectfully requested that the rejection be withdrawn since a proper prima facie case of obviousness has not been established based on the assembled references.

Conclusion

All of the stated grounds of rejections have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is hereby invited to telephone the undersigned at the number provided.

A Notice of Allowance with claims 2-19, 22-23, 27 and 28 is respectfully requested.

Respectfully submitted,

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